Remarks

The specification is amended herein to provide complete deposit information for the HuCC49V10 antibody, and ATCC Accession Numbers PTA-4182 and PTA-4183.

Claims 1-4, 6, 8, 10-12, 16, 20-28, 32-35, 44, 45, 47, 48, 52, 56, and 67 are pending in this application, of which claims 21, 22, 32-35, 44, 45, 47, and 48 are withdrawn. Claims 1, 20, 23, and 56 are amended herein and claim 56 is canceled. New claims 68-89 are added.

Support for the amendment of claim 1 can be found in the specification at least at page 23, Table 2 and in the attached deposit receipt (**Exhibit A**). Support for the amendment of claim 23 can be found in the specification at page 21, lines 15-17. Support for new claims 68-70 and 80-82 can be found in the specification at least at page 22, line 20 through page 23 and Table 2). Support for new claim 71 can be found in the specification at least at page 25, lines 18-19. Support for new claim 72 can be found in the specification at least at page 26, lines 3-7. Support for new claims 73-74, 78-79, 83-84, and 88-89 can be found in the specification at least at page 26, line 18 through page 27, line 3. Support for new claims 75 and 85 can be found in the specification at least at page 27, lines 5-20. Support for new claims 76-77 and 86-87 can be found in the specification at least at page 31, line 25 through page 33, line 23.

No new matter has been added by these amendments. Applicants reserve the right to pursue canceled or deleted subject matter in a continuing application. Unless specifically stated otherwise, none of the amendments made herein are intended to limit the scope of any claim. Reconsideration of the pending claims is respectfully requested.

Restriction Requirement

Applicants acknowledge that the election of Group I (claims 1-4, 6, 8, 10-12, 16, 20, 23-28, 52, 56, and 67) is made final and that claims 21, 22, 32-35, 44, 45, 47, and 48 are withdrawn.

Claim Rejections Under 35 U.S.C. §112, first paragraph

Claims 1, 20, 23, 56 and 67

Claims 1, 20, 23, 56 and 67 are rejected under 35 U.S.C. §112, first paragraph, as allegedly the specification is not enabling because it is "unclear if the CC49 antibody, HuCC49V10 antibody, and the nucleic acid sequence having the ATCC accession numbers PTA-4182 and PTA-4183 are known and publicly available, or can be reproducibly isolated without undue experimentation" (Office action at page 3). Claim 56 is canceled, rendering this rejection of the claim moot.

The CC49 monoclonal antibody is described in U.S. Patent Number 6,495,137 and its sequence is provided in this U.S. patent. Moreover, CC49 is expressed by a cell line deposited as ATCC Accession No. HB-9459 (see U.S. Patent Number 6,495,137 at column, 3 lines 4-5). Thus, the CC49 antibody is known and readily available to the public, and can be reproduced without undue experimentation.

Attached are two receipts from the American Type Culture Collection, which acknowledge that deposits were made in accordance with the Budapest Treaty. The first receipt (**Exhibit B**) identifies HuCC49V10-14, deposited as ATCC Accession No. PTA-4182 on March 26, 2002, and HuCC49V10-15, deposited as ATCC Accession No. PTA-4183 on March 26, 2002. The second receipt (**Exhibit A**) identifies HuCC49V10, deposited as ATCC Accession No. PTA-5416 on August 28, 2003. Thus, the HuCC49V10, HuCC49V10-14, and HuCC49V10-15 antibodies are known and readily available to the public, and reproducible without undue experimentation. All restrictions upon public access to ATCC Accession Nos. PTA-4182, PTA-4183, and PTA-5416 are irrevocably removed upon the grant of a patent, in accordance with the Budapest Treaty. In light of the above statements, the deposits, and the attached receipts, Applicants submit that all the conditions of 37 C.F.R 1.801-1.809 have been met.

As requested in the Office action, the specification is amended herein to provide complete deposit information by reciting the date of deposit and the complete name and address of the depository.

Reconsideration and withdrawal of this rejection of claims 1, 20, 23, 56 and 67 are respectfully requested.

Claims 1-4, 6, 8, 10-12, 16, 23-28, 52, 56, and 67

Claims 1-4, 6, 8, 10-12, 16, 23-28, 52, 56, and 67 are rejected as under 35 U.S.C. §112, first paragraph, as allegedly the specification does not reasonably provide enablement for the claimed humanized CC49 antibodies. Specifically, the Office action contends that the specification does not provide enablement for "any functional fragment of the humanized CC49 antibody" (claim 1) or "a variable light framework region and a variable heavy framework region of a human antibody" (claim 23; Office action at page 7). Applicants disagree. However, solely to advance prosecution in this case, claim 1 is amended to recite "an antigen binding fragment of the humanized CC49 antibody," as suggested by the Office action at page 6. Also solely to advance prosecution of this application, claim 23 is amended to recite "four variable light chain framework regions and four variable heavy chain framework regions," as suggested by the Office action at page 6. In light of the amendments of claims 1 and 23, Applicants respectfully request that these rejections of claims 1 and 23 (and the claims that depend therefrom) be withdrawn. Claim 56 is canceled, rendering this rejection of the claim moot.

The Office action also alleges that the specification does not reasonably provide enablement for a humanized CC49 antibody comprising "a non-conservative substitution at any position OR at any tyrosine residue of L-CDR3 OR substituting the tyrosine residue at position 91 with any amino acid, and wherein the humanized CC49 antibody had a high binding affinity for TAG-72, compared to a parent CC49 antibody" or a "non-conservative substitution of any residue in the L-CDR3 of the antibody; and a substitution of any residues in any L-CDR or H-CDR of the antibody; wherein the humanized CC49 antibody had a high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent CC49 antibody" (Office action, for example, at page 7). Applicants disagree.

The Federal Circuit has repeatedly stated that enablement is not precluded by the necessity for some experimentation, so long as the experimentation is not undue. *In re Wands,* 8

USPQ2d 1400 (Fed. Cir. 1988). A considerable amount of experimentation is permissible, if it is **merely routine**, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *Id.* Applicants submit that any experimentation would be routine and the present application provides the guidance necessary to prepare the claimed antibodies. For example, the specification describes the CC49 and HuCC49V10 antibodies. Moreover, the sequences of the CC49 and HuCC49V10 antibodies were well known at the time this application was filed (see Tamura *et al., J. Immunol.*, 164:1432-1441, 2000 – **Exhibit C;** PCT Application Nos. PCT/US89/04402 and PCT/US99/25552). It was also well known how to synthesize proteins, such as recombinant humanized antibodies, and make functional variants thereof. Furthermore, the specification explicitly teaches, and provides working examples, of the following:

(i) methods of generating a recombinant library of genes encoding antibody variants (page 34, line23 through page40, line 5);

(ii) methods of producing whole antibodies or Fab antibody fragments (page 40, lines 8 through page 42, line 8; page 45, line 10 through page 48, line 20);

(iii) methods of screening Fab antibody variants that bind to an antigen, for example, TAG-72 (page 40, lines 8 through page 45, line 8); and

(iv) methods of testing variant whole antibodies for antigen binding activity and immunoreactivity (page 47, line 1 through page 48, line 2; page 48, line 22 through page 53, line 23).

In fact, the specification discloses the synthesis and testing of multiple antibody variants, in addition to the HuCC49V10-14 and HuCC49V10-15 antibodies. Based on the binding affinity and immunogenicity testing disclosed in the specification, Applicants determined whether a variant antibody had high binding affinity for TAG-72 and/or minimal immunogenicity, compared to a parent CC49 antibody. Thus, as evidenced by the teachings of the specification and the knowledge of one of skill in the art at the time the application was filed, it would be simply a matter of **routine** to (i) make humanized CC49 antibodies having the claimed genus of residue substitutions and (ii) test these antibodies for their binding affinity and immunogenicity.

Applicants further submit that, contrary to the assertion of the Office action (page 16), such experimentation would not be undue. In light of the above discussion, Applicants submit that the claims, as amended, are fully enabled by the specification and respectfully request that the rejection of claims 1-4, 6, 8, 10-12, 16, 23-28, 52, 56, and 67 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claim Rejection Under 35 U.S.C. §112, second paragraph

Claim 56 is rejected under 35 U.S.C. §112, second paragraph, as allegedly vague and indefinite for reciting the term "HuCC49V10." As discussed above, claim 56 is canceled, rendering this rejection of claim 56 moot. Applicants respectfully request that this rejection of claim 56 be withdrawn.

Request for Rejoinder

The Examiner has required a restriction between product and process claims. The Applicants have elected claims to a specific product. In accordance with M.P.E.P. § 821.04, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined. Applicants expressly request that the method claims be rejoined and the claims examined, at the latest upon the allowance of any of the product claims. It is believed that this is in accordance with the current Patent and Trademark Office Guidelines for Restriction Requirements in TC1600.

Conclusion

It is respectfully submitted that the amended composition claims as pending should be allowed, and that the pending method claims should be recombined with the composition and considered in the current case. If any matters remain to be addressed before a Notice of Allowance is issued, the Examiner is formally requested to contact the undersigned prior to issuance of the next Office action, in order to arrange a telephonic interview. It is believed that a brief discussion of the merits of the present application may expedite prosecution. This request is being submitted under MPEP §713.01, which indicates that an interview may be arranged in advance by a written request.

Respectfully submitted,

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